

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
19 May 2005 (19.05.2005)

PCT

(10) International Publication Number
WO 2005/045066 A1

- (51) International Patent Classification⁷: C12Q 1/25, (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (21) International Application Number: PCT/US2004/035719
- (22) International Filing Date: 28 October 2004 (28.10.2004)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data: 60/515,012 28 October 2003 (28.10.2003) US
- (71) Applicant (for all designated States except US): SERENEX, INC. [US/US]; 323 Foster Street, Durham, NC 27701-2102 (US).
- (72) Inventor; and
- (75) Inventor/Applicant (for US only): PARTRIDGE, Jeffrey, M. [US/US]; 4905 Linden Oaks Ave., Durham, NC 27713 (US).
- (74) Agents: COULTER, Kathryn, L. et al.; Alston & Bird LLP, Bank of America Plaza, Suite 4000, 101 South Tryon Street, Charlotte, NC 28280-4000 (US).
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:
- with international search report
 - before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: FOLATE ANTAGONISTS HAVING IMPROVED SELECTIVITY

(57) Abstract: The present invention provides methods for identifying improved folate antagonists. The improved folate antagonists identified by the methods of the invention have increased selectivity. The increased selectivity of the folate antagonists results in a reduced risk of adverse effects following treatment with the improved folate antagonists. The improved folate antagonists are identified based on their reduced binding affinity for at least one enzyme selected from glutathione synthase, pyruvate carboxylase, propionyl-CoA carboxylase, biotin carboxylase, acetyl-CoA carboxylase, and methylcrotonyl-CoA carboxylase. According to the invention, folate antagonists having reduced affinity for at least one enzyme selected from this group of enzymes are selected for the treatment of neoplastic hyperproliferative, and immune disorders.



WO 2005/045066 A1